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*Review Article*

# Application progress on construction of quality management system for blood group genotyping

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## ABSTRACT

In transfusion medicine, DNA-based genotyping is rapidly being employed as an alternative to serological antibody-based methods for blood group determination in donor-recipient matching, becoming a crucial method for precise blood typing. Currently, there is a lack of unified quality management norms, including quality control and quality assurance programs, as well as standard operating procedures (SOPs) related to blood genotyping technology. The blood genotyping quality management system (QMS) serves as the core framework to ensure the accuracy of genotyping results and the safety of clinical samples, covering key dimensions such as technical standards, personnel competency, equipment management, data security, and sample compliance. Blood genotyping quality management provides a systematic strategy and direction for quality control, while quality control implements the objectives of quality management through specific technical measures. The combination of both forms a closed-loop management system of "prevention-control-improvement", covering the entire process: pre-testing, under testing, and post-testing phases. By integrating relevant regulations and work practices, this paper conducts an initial application focusing on the QMS framework and standards, quality control of key processes, personnel and facility requirements, data security and sample safety compliance, as well as continuous improvement and future development.

**Keywords:** blood type, genetic testing, quality management, external quality assessment, blood transfusion safety, precision medicine

## INTRODUCTION

Blood group genotyping is a modern biological method that identifies blood groups through analysis of an individual's genomic information. Advancements in molecular biology and genetics have enabled DNA-based molecular methods to provide robust technical support for fields such as clinical medicine, forensic science, and paternity testing. Compared with traditional serological methods, blood group genotyping is more complex and involves numerous manual operational steps. Data analysis and variant interpretation are highly dependent on bioinformatics analysis, and there are significant differences in the bioinformatics capabilities among different laboratories. Currently, there remains a lack of mature

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commercial reagents for high-throughput sequencing both domestically and internationally. Each laboratory uses independently developed testing methods, lacking standardized protocols and unified testing criteria, which poses great challenges to quality assurance of genotyping results. In addition, the identification of difficult blood groups increasingly relies on the results of genetic testing. Therefore, the accuracy of genetic testing results may directly influence clinical diagnosis and treatment. The quality management system (QMS) for blood group genotyping serves as the core framework ensuring testing accuracy and clinical safety, covering key dimensions including technical standards, personnel competency, equipment management, data security, and sample compliance. Quality management establishes systematic strategies to guide quality control, while quality control implements specific technical measures to achieve management objectives. Together, they form a closed-loop "prevention-control-improvement" management cycle encompassing the entire process from pre-analytical preparation to post-analytical evaluation. In accordance with relevant regulations and practical work experience, this paper presents a preliminary exploration of the following aspects: the QMS framework and standards, quality control of key processes, personnel and facility requirements, data security and sample safety compliance, as well as continuous improvement and future development.

## QMS FRAMEWORK AND STANDARDS

### Documented management system

It is essential to establish comprehensive documentation covering the entire quality management cycle, including quality manuals, procedural protocols, regulations, standard operating procedures (SOPs), safety guidelines, and record-keeping systems. These documents should undergo regular review and updating, with obsolete versions promptly archived to maintain current validity. Key elements, including laboratory culture, critical management systems, personnel responsibilities, infection control protocols, fire safety measures, and emergency response plans, should be displayed on bulletin boards in public corridors. Each laboratory workstation features visual guides detailing basic instrument operation, reagent preparation, and experimental procedures. Documented workflows and accountability mechanisms eliminate risks associated with subjective decision-making, ensuring full-process traceability and guaranteeing test accuracy and reliability – essential requirements for accreditation under standards such as ISO15189 and CNAS-CL02. Through systematic documentation and internal audits, continuous improvement opportunities are identified to enhance laboratory management. The documented management system forms the foundation for standardized, internationally compliant operations, anchored by the core principle of "documented evidence and verifiable records" to ultimately achieve the goal of "delivering high-quality clinical testing services to patients" (***Fig. 1***).

### Information management system

The Laboratory Information Management System (LIMS) is an integrated framework that combines information technologies with laboratory workflows to achieve automated testing data processing, standardized procedures, and evidence-based decision-making. Our developed blood group and genetic testing LIMS features modules including sample management, testing workflow management, report management, equipment management, data management, quality control, and specimen repository management. It encompasses specimen entry (*via* local input or mobile APP), review and handover (logistics and specimen information), specimen testing (project allocation, sub-project layout, and stepwise testing), report review (value generation, image upload, merging/splitting), report inquiry (internal queries, client inquiries, progress tracking, and final reports), and post-test specimen management (including DNA) covering destruction, storage, and external delivery. The system manages personnel, equipment, specimens, and reagents throughout the entire process. It utilizes Radio Frequency Identification (RFID) and barcode technology for unique identification, enabling full-process traceability from collection, registration, and storage to disposal, with automatic expiration processing. The testing process is fully controlled, with automatic sample assignment to corresponding testing teams based on project requirements, supporting multi-channel client and business-end commissioning. Built-in quality control rules enable real-time monitoring of testing processes to ensure compliance with ISO15189 and ISO/IEC17025 standards. Reports and data analysis are generated through human-machine collaboration, supporting review, printing, and electronic transmission. The system provides trend analysis, statistical reports, and visual dashboards to assist in quality improvement and decision-making. Equipment and consumables management, along with equipment network monitoring enable real-time

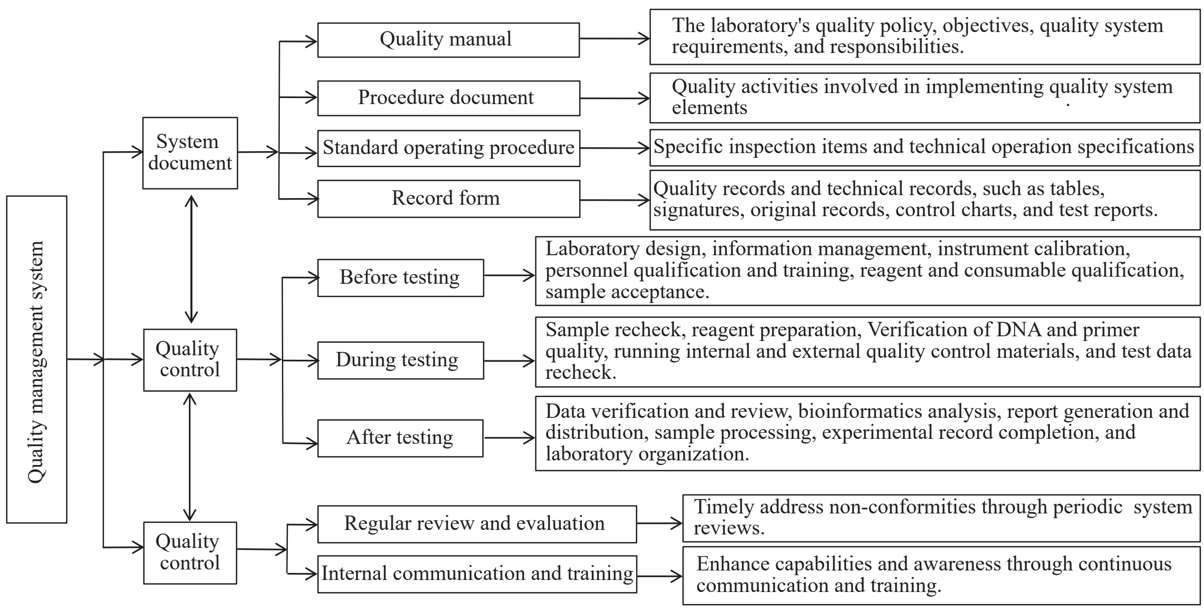


***Fig. 1*** **Quality management system**

tracking of instrument status and support preventive maintenance and calibration schedules. Intelligent management of reagent consumables involves RFID tags to record expiration dates and storage conditions, predict consumption, and generate purchasing plans (***Fig. 2***).

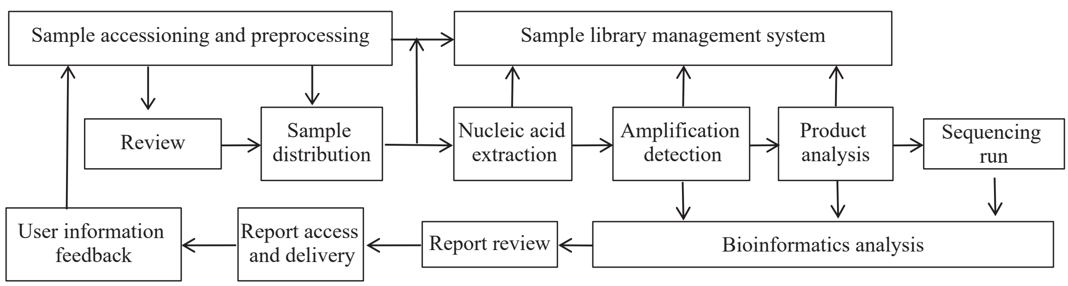


***Fig. 2*** **Flowchart of the blood group genotyping information management system**

### Compliance with standard requirements

This article was developed in compliance with a range of national regulations and guidelines, including the "Management Measures for Clinical Laboratories of Medical Institutions", "Management Measures for Clinical Gene Amplification Testing Laboratories of Medical Institutions", "Law of the People's Republic of China on the Prevention and Treatment of Infectious Diseases", "Regulations on Biosafety Management of Pathogenic Microorganism Laboratories", "CNAS-GL029 Guidelines for Accreditation of Detection Laboratories in the Field of Gene Amplification", "WS/T 230-2024 Guidelines for Implementation of Real-time Fluorescent Polymerase Chain Reaction in Clinical Laboratories"[1], as well as relevant provincial management regulations. It is suggested to consult internationally recognized laboratory construction standards to establish a quality system that promotes continuous improvement and facilitates successful technical acceptance by the designated management department.

## QUALITY CONTROL OF KEY PROCESSES

### Pre-testing phase management

#### Sample management

Sample collection must be standardized, with ethylenediaminetetraacetic acid (EDTA) or Acid-Citrate-Dextrose (ACD) anticoagulated venous blood preferred to avoid heparin-induced inhibition of Polymerase Chain Reaction (PCR) reactions. The minimum submission volume for anticoagulated whole blood should be at least 3 mL. In most cases, a recent blood transfusion history does not affect molecular biology testing. Sample transportation must be conducted in a manner that prevents leakage and contamination. Blood samples stored at 4 ℃ should not exceed 72 hours to avoid hemolysis or contamination. DNA extraction requires purity and integrity verification. For blood group genotyping, the minimum required DNA sample concentration is ≥ 10 ng/μL, with purity meeting $OD_{260}/OD_{280} = 1.8 \pm 0.2$[2]. Cold chain transportation using dry ice or liquid nitrogen ensures DNA stability, and external delivery must comply with biosafety packaging standards. Samples must be uniquely coded and labeled to match application form information for full traceability. Test applications should align with clinical information, including the subject's blood transfusion history, pregnancy status, medication history (antibodies), clinical diagnosis, and serological test results. Informed consent must be obtained when required.

**Reagent management**

Strict qualification reviews must be enforced for the issuance of medical device production and operation licenses to suppliers. Additionally, stringent zoning protocols for storage should be implemented to prevent the reverse flow of materials to front-end areas. The core of DNA extraction lies in releasing DNA through cell lysis, removing impurities such as proteins, RNA, salts, and capturing/purifying DNA *via* physical or chemical separation methods.. The extracted DNA must meet downstream experimental requirements (*e.g.*, $OD_{260}/OD_{280}$ = 1.7–1.9 for PCR, concentration ≥ 50 ng/μL, high-purity DNA for sequencing)[3]. The essence of DNA amplification is *in vitro* replication of target DNA fragments such as PCR or whole genome amplification. which requires specificity (primer design), efficiency (enzyme activity), and fidelity (low mutation rate). Core product analysis involves verifying amplification results (*e.g.*, fragment size, concentration, and purity), using common methods including electrophoresis (agarose/capillary) and real-time quantitative PCR (qPCR). The essence of sequencing lies in determining DNA sequences *via* techniques such as Sanger sequencing or high-throughput sequencing, ensuring high sequencing quality (free from impurity interference) and sufficient signal intensity (adequate template quantity). Protease K should be stored at −20 ℃, and elution buffer pH must be ≥ 8.0 to prevent DNA degradation. All reagents must be nuclease-free (DNase/RNase-free). For consumables management, batch quality inspection reports and sterility certificates should be verified upon acceptance. New batches must undergo blank control tests prior to initial use to confirm no nucleic acid contamination. Gene detection consumables, such as enzyme-free pipettes and low-adhesion EP tubes, must be labeled as "DNase/RNase-free". All laboratory areas must be equipped with filter-equipped pipettes for the aspiration of samples or nucleic acid-containing solutions during operations. Supervision should be strengthened by maintaining electronic records documenting consumable usage, opening dates, handlers, and remaining quantities, with regular inventory checks performed. Single-use consumables must not be reused and should undergo autoclaving as biological hazard waste after experiments.

**Personnel qualifications**

Laboratory technicians are required to possess a valid Medical Laboratory Technician Qualification Certificate. Laboratory directors should possess at least a bachelor's degree, intermediate or senior professional titles, and a minimum of three years of experience in genetic testing or related fields. The laboratory must employ sufficient personnel (at least two individuals per testing category) who have completed training programs authorized by provincial-level authorities or the National Health Commission (NHC). These staff members must hold certificates in clinical gene amplification testing, specialized classification programs, biosafety protocols, large medical equipment operation, and bioinformatics analysis. The laboratory should ensure regular training for all staff, including internal and external programs, maintain annual training plans with documentation, and conduct pre-employment training and assessments for new hires or personnel returning after an absence of more than six months. Regular evaluations (at least annually) of technicians' capabilities should be conducted, including theoretical assessments, experimental proficiency tests, and quality control comparisons. The laboratory must maintain technical records for all personnel, including resumes, health status updates, qualification certificates (such as academic degrees, professional titles, and certification credentials), training documentation, theoretical and practical assessments, and research publications[4–5].

## In-process technical control

**Method validation**

When employing technologies such as PCR, gene chips, Sanger sequencing, or single-molecule sequencing, parameters including precision, contamination rate, and comparability must be validated. PCR primer design should cover target gene mutation sites (*e.g.*, the C-258 deletion in the *ABO* gene) and undergo specificity validation. Strict optimization of annealing temperatures (*e.g.*, 60 ℃), cycle numbers (*e.g.*, 35 cycles), and reaction systems is required, with negative/positive controls as well as external quality controls established for each batch. Enzymatic digestion (*e.g.*, 37 ℃ digestion with *KpnI* and *AluI* for 3 hours) must be periodically validated, and electrophoresis results must be standardized through gel imaging system interpretation. Genotyping outcomes should align with serological typing results (*e.g.*, combined with ABO positive/negative typing), and any discrepancies require repeat testing or confirmation by sequence-specific primer PCR (PCR-SSP). Complex samples, such as those with ABO subtypes, require re-verification using multiplex PCR or sequencing technologies. Original data from third-generation sequencing platforms (*e.g.*, Oxford Nanopore or PacBio) must meet the following quality control metrics: an N50 read length > 10 kb, and a mean quality score (Q-score) > 7. Standardized software should be employed for sequence analysis, with mutation sites meeting a minimum read depth (DP) of ≥ 20 × and a Q-score of ≥ 30[6].

**Equipment calibration and maintenance**

It is important to establish comprehensive equipment records detailing serial numbers, locations, calibration schedules, and historical data. Calibration institutions should prioritize laboratories accredited by the China National Accreditation Service (CNAS) to ensure calibration coverage for all equipment types such as biosafety cabinets requiring high-efficiency particulate air (HEPA) filter leak testing. Core equipment must undergo regular calibration. Biosafety cabinet calibration includes measurements of vertical airflow velocity, airflow direction/velocity within the work chamber, HEPA filter leak testing (poly-alpha-olefin, PAO test), particulate matter, noise, illuminance, and airborne/sedimentary microbial counts. Calibration frequencies should be performed after installation, relocation, or maintenance/HEPA filter replacement, in addition to at least one routine check annually. Immediate contamination control is required if sedimentary bacteria exceeds 1 CFU/plate. Pipette calibration involves measuring actual mass using standard weights and calculating error (formula: Error (%) = (Actual Mass − Reference Value) / (Reference Value × 100)). Errors exceeding 1% require adjustment. Calibration should be conducted every 1–3 months, with increased frequency for high-frequency users. Multi-channel pipettes require calibration of each individual channel. Centrifuge calibration covers rotational speed (RPM/RCF, with errors ≤ 5%), temperature fluctuation (± 0.5 ℃), timing accuracy, and rotor balance. Annual calibration is mandatory, while high-speed models or frequently used units should be calibrated every 6 months. Refrigerated centrifuges require verification of temperature uniformity (*e.g.*, −20 ℃ ± 2 ℃). PCR instrument calibration focuses on inter-well temperature uniformity, heating/cooling rates, thermal lid pressure, and fluorescence channel sensitivity (qPCR). Annual calibration is required, with gradient PCR instruments needing additional gradient accuracy verification. The sequencing instrument calibration program covers optical systems (fluorescence signal intensity), fluid control systems, temperature modules, and base recognition accuracy. Calibration is performed follwoing manufacturer manuals (typically every 3–6 months), with verification required after each chip or reagent batch replacement. The refrigerator/freezer calibration program includes verification of temperature stability (*e.g.*, ± 2 ℃), uniformity, and alarm functionality. Calibration is conducted every 6–12 months, with particular attention to monitoring temperature fluctuations in ultra-low temperature freezers (−80 ℃).

**Internal quality control**

Each batch of testing requires blank, positive, and negative control samples to monitor stability. The blank control excludes DNA contamination from reagents, environment, or operator handling in blood group gene detection methods such as PCR sequencing and qPCR[7], verifying the reagent purity and ensuring baseline reliability. The negative control prevents false positives caused by non-specific amplification such as primer binding to non-target genes. The positive control validates method effectiveness and calibrates experimental conditions. By monitoring signal intensity (*e.g.*, PCR product yield, fluorescence values), parameters including cycle numbers and template amounts can be adjusted to ensure sensitivity, for instance, in detecting low-concentration target genes. Blood group gene detection kits utilize internal reference primers to verify the successful extraction of samples[8]. Abnormal amplification curves or cycle threshold (Ct) values (excessively high) may indicate sample degradation, failure in RNA/DNA extraction, or reverse transcription issues. In quantitative experiments, reference primers correct sample variations, such as differences in template concentration and pipetting errors, by calculating ΔCt values between target and reference primers, thereby enhancing result accuracy. These primers facilitate the interpretation of results: the amplification of normal reference genes (with undetected target gene amplification) rules out experimental system issues and confirms no target gene expression. It should be noted that reference primers cannot substitute for positive/negative controls.

**Third-party quality control products**

External quality control materials (also known as "inter-laboratory quality control materials") are reference materials provided by third-party institutions with known blood group and genotype information (such as specific ABO and Rh alleles). These materials are used in cross-laboratory quality assessment to verify whether participating laboratories can accurately identify common blood types (*e.g.*, A, B, O, and Rh-positive) and rare phenotypes (*e.g.*, Rh-negative, Bombay type, and weak A/B subtypes). For instance, if a laboratory misidentifies Rh-negative status using external quality control materials, it indicates potential issues in testing methods or operational execution that necessitate correction. External quality control materials can detect inter-laboratory inconsistencies in results (such as variable identification of the same rare blood type), ensuring transfusion safety, as incorrect blood type identification may cause hemolytic transfusion reactions. For newly developed blood group genetic testing projects (*e.g.*, rare blood type genotyping), external quality control materials can validate methodological accuracy, for example, by confirming consistency with international standards. The four components collectively form a quality control system for blood group genetic testing: blank controls prevent contamination; negative controls prevent false positives; positive controls prevent false negatives; and external quality control materials ensure inter-laboratory consistency and accuracy. Together, these components guarantee the accuracy, specificity, and sensitivity of test results, ultimately promoting transfusion safety (*e.g.*, avoiding incompatible blood transfusions) and clinical diagnostic reliability (*e.g.*, screening for hemolytic disease of the newborn).

## Post-testing analysis

**Bioinformatics analysis**

Standardized workflows are implemented for data comparison and annotation, combined with AI-enhanced variant interpretation[9]. Raw data of blood group systems (*e.g.*, *ABO*, *RhD*/*RHCE*, and *MNS*) are generated using second-/third-generation high-throughput sequencing technologies. Quality control tools such as FastQC or SOAPnuke filter out low-quality sequences, adapter contamination, and repetitive reads to ensure data reliability. Sequencing data are aligned to the human reference genome (*e.g.*, hg38)[10] using BWA[11] or Bowtie2[12] to locate target gene regions. Single nucleotide polymorphism (SNP) detection, insertion and deletion (Indel) identification, copy number variation (CNV) analysis, and structural variation (SV) mapping are performed through GATK4[13–14] and Samtools[15]. Key variants identified include *c.261delG* (O-type) in the *ABO* gene and *RHD* deletion (Rh-negative) in the *RhD* gene. The clinical significance of variants is annotated using public databases such as dbSNP and ClinVar, alongside specialized blood group databases (*e.g.*, International Society of Blood Transfusion, ISBT). Antigen expression prediction, such as the GP (A-B) fusion antigen within the MNS system, is conducted *via* the BloodTyper software[16].

**Result verification**

A two-person review mechanism ensures accuracy. This dual-check process serves as a critical quality control measure, reducing human error through independent verification and enhancing result precision. This mechanism must be applied in high-risk scenarios, with particular emphasis on the following situations: complex blood type testing involving rare blood types like Bombay-like type, Ael subtype, and Rhnull (golden blood type); genetic mutation findings including *ABO* locus mutations (*e.g.*, *CisAB* and *B(A)* subtypes) and *RhD* gene deletion/mutation (e.g., *weak D* type); conflicting results between serological testing and genotyping outcomes (*e.g.*, serologically typed as O type but genetically detected as A/B type); and critical clinical cases such as emergency transfusion requirements, organ transplant recipients, or parentage dispute cases. All blood group genotyping results must undergo dual-person review following a standardized workflow: initial recording → independent review → result confirmation → anomaly handling. This process must be carried out by qualified personnel in compliance with industry standards to provide reliable evidence for clinical decision-making[17].

## Personnel and facility requirements

**Personnel configuration requirements**

The laboratory must maintain a technical staff composition of at least 75% with bachelor's degrees or higher, including laboratory directors with clinical medicine backgrounds. Technical personnel should demonstrate proficiency in laboratory medicine, genetics, molecular biology, and core technologies like PCR, electrophoresis, and gene sequencing. All staff are required to possess certification as amplification laboratory technicians and to complete specialized training in blood group genotyping. Quality management necessitates the appointment of a dedicated quality supervisor responsible for reagent validation, equipment calibration, and compliance reviews. Report interpreters must possess expertise in clinical transfusion medicine and bioinformatics to make comprehensive judgments based on serological results[5].

**Laboratory environment**

The laboratory facility must comply with Biosafety Level 2 (BSL-2) standards and equipped with BSL-2 fume hoods, emergency eyewash stations, and autoclaving equipment. Environmental parameters shall be strictly controlled, with temperature maintained between 20 ℃ and 25 ℃, relative humidity below 80%, and ambient noise levels not exceeding 70 dB to avoid interference with precision instruments. Regular microbial monitoring shall be performed. A zoned management system shall be implemented as a critical contamination control measure, which physically separates the laboratory into dedicated areas for reagent preparation, sample processing, amplification, product analysis, and sequencing. Each zone maintains independent ventilation with unidirectional pressure gradients (decreasing from reagent area to analysis area). Movement of personnel, materials, and samples must follow a unidirectional workflow, preventing any reverse cross-flow. Infection-related waste must undergo autoclaving at 121 ℃ for more than 30 minutes prior to removal from the laboratory.

## Data security and sample security

**Gene detection data security**

To ensure the security of blood type genetic testing data, PCR instruments and sequencers must be dedicated for specific purposes during testing. The blood type genetic testing information management system operates independently, maintaining complete isolation from the internet. Following the generation of sequencing data, encrypted transmission is conducted using hard drives or similar media, with passwords delivered through separate channels from the data. Additionally, due to the massive volume of data, MD5 codes are generated before transferring the data to storage media to prevent errors during transmission. Upon receipt of the data at the destination, the MD5 code is verified again to ensure integrity and accuracy[18]. Given the high cost and irreproducibility of sequencing, a "two-site, three-center" disaster recovery backup solution must be established.

**Sample safety**

The samples utilized for blood type genetic testing and intermediate products from sequencing processes contain human genetic material and require proper storage. After experiments, peripheral whole blood and extracted genomic DNA must be processed according to established protocols. Samples designated for disposal must undergo high-pressure sterilization at 121 ℃ for more than 30 minutes before removal from the laboratory. Samples (including DNA) intended for external transportation must be properly packaged and transported *via* cold chain. Stored samples (including DNA) should be arranged in standardized specimen storage boxes and managed in accordance with the operational manual of the specimen database information management system. The blood type genetic testing information management system ensures effective control over all stages of sample (DNA) handling, including receipt, redistribution, and post-processing, throughout the entire process, safeguarding sample integrity (***Fig. 3***).

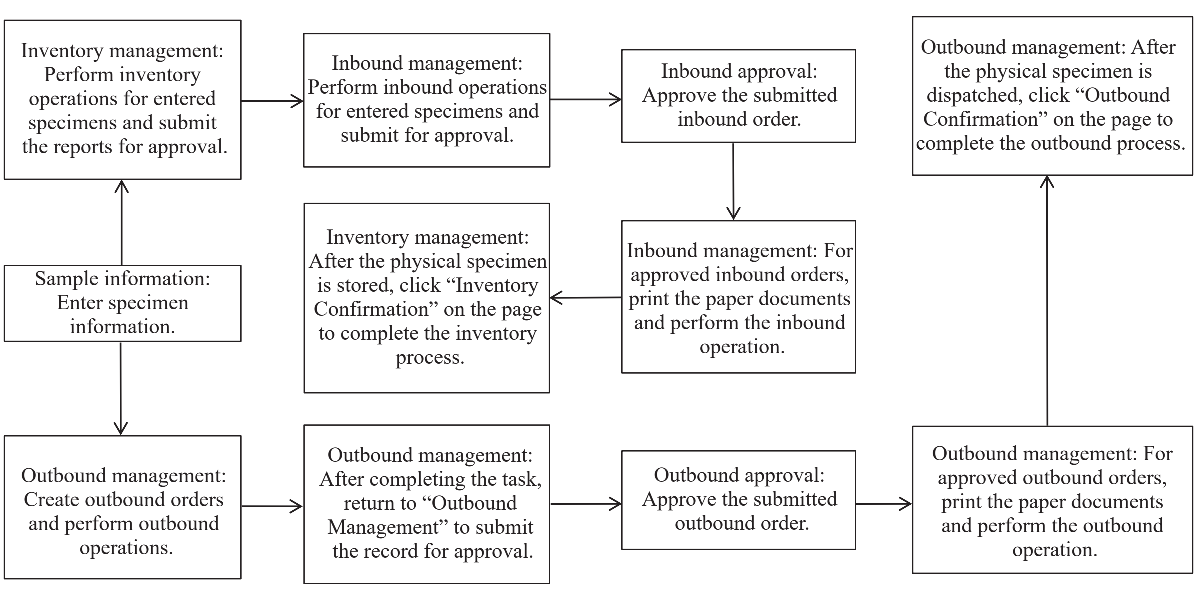


***Fig. 3*** **Sample library management information system**

## CONTINUOUS IMPROVEMENT AND FUTURE DEVELOPMENT

The application of technologies such as multiplex PCR and PCR-SSP has enabled simultaneous amplification of multiple genetic loci, significantly improving detection throughput. When combined with fluorescence labeling and real-time quantitative techniques, these advancements further enhance detection sensitivity and specificity. Through the integration of nanotechnology and bioinformatics, the miniaturization and intelligence of gene chips have increased detection site density and simplified operational procedures, allowing simultaneous testing of multiple blood group systems (*e.g.*, ABO, Rh, and MNS) for large-scale population screening. High-throughput sequencing technologies such as Illumina and PacBio, leveraging their advantages of "high throughput, high accuracy, and low cost", have become crucial tools in blood type gene testing. Their long-read capabilities enable precise identification of rare blood group gene mutations, resolving complex typing issues that are undetectable by traditional methods[19–21]. From phenotypic verification (serology) to genetic analysis (PCR-SSP, first-, second-, and third-generation sequencing), this study ultimately focuses on molecular mechanisms (protein modeling) and functional prediction, reveals the impact of mutations on antigen expression, and establishes a complete evidence chain for research on blood group antigen mutation[22–24].

The deep integration of bioinformatics and AI optimizes gene sequence alignment algorithms through big data analysis, reducing false-positive/false-negative results. AI such as machine learning automatically interprets complex genetic data, improving result interpretation efficiency and reducing reliance on specialists. Gene testing technologies will be more widely applied in the screening and identification of rare blood types, which helps expand blood bank resources and provide compatible blood sources for patients with rare blood types, such as those requiring emergency blood transfusions or major surgeries, thereby reducing transfusion risks. The automation and intelligent development of blood group analyzers, PCR instruments, gene chip systems, and sequencers have enabled full automation from sample preparation to result output in blood type gene testing. Participation in domestic and international quality assessment programs, such as those provided by the European Molecular Genetics Quality Network (EMQN) and the National Center for Clinical Laboratories (NCCL), validates inter-laboratory consistency. This initiative will drive international organizations like the World Health Organization (WHO) and the International Council for Standardization in Haematology (ICSH) to establish standards for blood type genomics testing, including standardized methodologies and interpretation protocols, thereby enhancing global testing consistency. With the deepening application of AI and big data technologies, AI techniques such as deep learning can be employed to analyze massive genetic datasets and uncover new functions of blood type genes (*e.g.*, their associations with diseases)[25]. The integration of multi-source information, including clinical and environmental data, enables dynamic monitoring and prediction of blood type genes. Furthermore, the integration of multi-omics data, combining genomics, transcriptomics, and proteomics, helps validate the functional impacts of genetic variants and enables the investigation of interactions between blood type genes and diseases (*e.g.*, cancer and cardiovascular disorders) or environmental factors (*e.g.*, drug responses), providing evidence for personalized treatment[26–27].

The ongoing advancements and future development of blood type genetic testing will provide stronger safeguards for human health through technological integration, such as AI, big data, and multi-omics, expanded applications in areas such as transfusion medicine and personalized medicine, standardization, and international collaboration. In the coming years, continuous technological advances are expected to establish blood type genetic testing as a crucial pillar of precision medicine, offering new hope to a greater number of patients.

### Author contributions

Software, Jieyin Chen; Validation, Enxiang Shi and Jieyin Chen; Writing – Original Draft Preparation, Enxiang Shi and Jieyin Chen; Writing – Review & Editing, Enxiang Shi; Visualization, Jiyuan Liu; Project Administration, Jiyuan Liu.

### Ethics statement

Not applicable.

### Informed consent statement

Not applicable.

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## Declaration of competing interest

The authors declared no conflict of interests.

### References


[1] National Health Commission of the People's Republic of China. Guidelines for implementation of real-time fluorescent polymerase chain reaction in clinical laboratories: WS/T 230-2024[S/OL]. [2024-11-01]. https://www.nhc.gov.cn/cms-search/downFiles/6c086be414ad4c13-befdf77c033537c5.pdf.

[2] Mullegama SV, Alberti MO, Au C, et al. Nucleic acid extraction from human biological samples[J]. *Methods Mol Biol*, 2019, 1897: 359−383.

[3] Carpi FM, Di Pietro F, Vincenzetti S, et al. Human DNA extraction methods: patents and applications[J]. *Recent Pat DNA Gene Seq*, 2011, 5(1): 1–7.

[4] Ministry of Health of the People's Republic of China. Management measures for clinical gene amplification testing laboratories in medical institutions[S/OL]. [2010-12-06]. https://www.nhc.gov.cn/zwgkzt/pyzgl1/201012/49981.shtml.

[5] Jiangsu Commission of Health. Jiangsu Province Clinical Gene Amplification Testing Technology Management Standards (Trial)[S/OL]. [2010-06-24]. https://wenku.baidu.com/view/4ec2222468dc5022aaea998fcc22bcd126ff429d.html?_wkts_=1764577886857.

[6] Lu Y, Li G, Wang Y, et al. Expert consensus on clinical genome sequencing interpretation and reporting[J]. *Hereditas (Beijing)* (in Chinese), 2025, 47(3): 314–328.

[7] Zhang F, Flickinger M, Taliun SAG, et al. Ancestry-agnostic estimation of DNA sample contamination from sequence reads[J]. *Genome Res*, 2020, 30(2): 185−194.

[8] Raymaekers M, Smets R, Maes B, et al. Checklist for optimization and validation of real-time PCR assays[J]. *J Clin Lab Anal*, 2009, 23(3): 145−151.

[9] Luan H, Niu B. Genome variation detection and analysis process[J]. *Front Data Comput*, 2024, 6(5): 139−147.

[10] Kendig KI, Baheti S, Bockol MA, et al. Sentieon DNASeq variant calling workflow demonstrates strong computational performance and accuracy[J]. *Front Genet*, 2019, 10: 736.

[11] Li H, Durbin R. Fast and accurate long-read alignment with Burrows-Wheeler transform[J]. *Bioinformatics*, 2010, 26(5): 589−595.

[12] Liu WJ, Liu P, Lei W, et al. Surveillance of SARS-CoV-2 at the Huanan Seafood Market[J]. *Nature*, 2023, 631(8020): 402−408.

[13] McKenna A, Hanna M, Banks E, et al. The Genome Analysis Toolkit: a MapReduce framework for analyzing next-generation DNA sequencing data[J]. *Genome research*, 2010, 20(9): 1297−1303.

[14] Geraldine A. Van der Auwera and Brian D. O'Connor. Genomics in the Cloud: Using Docker, GATK, and WDL in Terra[M]. CA: O'Reilly Media, 2020.

[15] Li H, Handsaker B, Wysoker A, et al. The Sequence Alignment/Map format and SAMtools[J]. *Bioinformatics*, 2009, 25(16): 2078−2079.

[16] Halls JBL, Vege S, Simmons DP, et al. Overcoming the challenges of interpreting complex and uncommon RH alleles from whole genomes[J]. *Vox Sang*, 2020, 115(8): 790−801.

[17] Hu J, Lin Y, Xia R, et al. Clinical practice of ABO blood group molecular analysis: Chinese expert consensus[J]. *Blood Genom*, 2023, 7(2): 77−85.

[18] Liu Y, Xu Z, Cheng S, et al. Clinical research-oriented gene sequencing projects: rationale, management and quality control standards[J]. *Chin J Stroke* (in Chinese), 2022, 17(3): 227−235.

[19] Yang H, Guan Y, Ma X, et al. Pedigree analysis of Bel subtype caused by the new allele c.175_176insGA[J]. *Chin J Lab Med* (in Chinese), 2024, 47(10): 1206−1211.

[20] Chen L, Zhang Y, Che J, et al. Analysis of ABO serological phenotype and molecular biology results of 256 blood donors with ambiguous blood group[J]. *Chin J blood Transfus* (in Chinese), 2024, 37(7): 766−772.

[21] Shen X, Yang J, Xu C, et al. Construction and implementation of artificial intelligence-based blood transfusion decision support system[J]. *Chin J Health Inform Manag* (in Chinese), 2021, 18(4): 455–459.

[22] Lei H, Zheng J, Xiang D, et al. The -72G>A nucleotide substitution impairs transcription of the ABO gene *via* reduction of promoter activity[J]. *Blood Transfus*, 2025, 23(2): 118−122.

[23] He Y, Yu L, Zhang J, et al. Serological and molecular characterization of novel ABO variants including an interesting B(A) subgroup[J]. *Transfusion*, 2024, 64(12): 2364−2370.

[24] Xia Y, Shao L, Li N, et al. Identify the CisAB subtype by PacBio third-generation sequencing technology and explore the molecular mechanism by molecular docking[J]. *J Clin Transfus Lab Med* (in Chinese), 2024, 26(6): 792−796.

[25] Moslemi C, Sækmose S, Larsen R, et al. A deep learning approach to prediction of blood group antigens from genomic data[J]. *Transfusion*, 2024, 64(11): 2179−2195.

[26] Gleadall NS, Koets L, Shamardina O, et al. Array genotyping of transfusion-relevant blood cell antigens in 6946 ancestrally diverse study participants[J]. *Blood*, 2025, 146(12): 1511−1524.

[27] Zhu X, Guo B, Zhang J. Research on correlation of ABO blood group distribution in patients withrectal malignant tumors[J]. *J Bengbu Med Univ* (in Chinese), 2025, 50(6): 797−805.